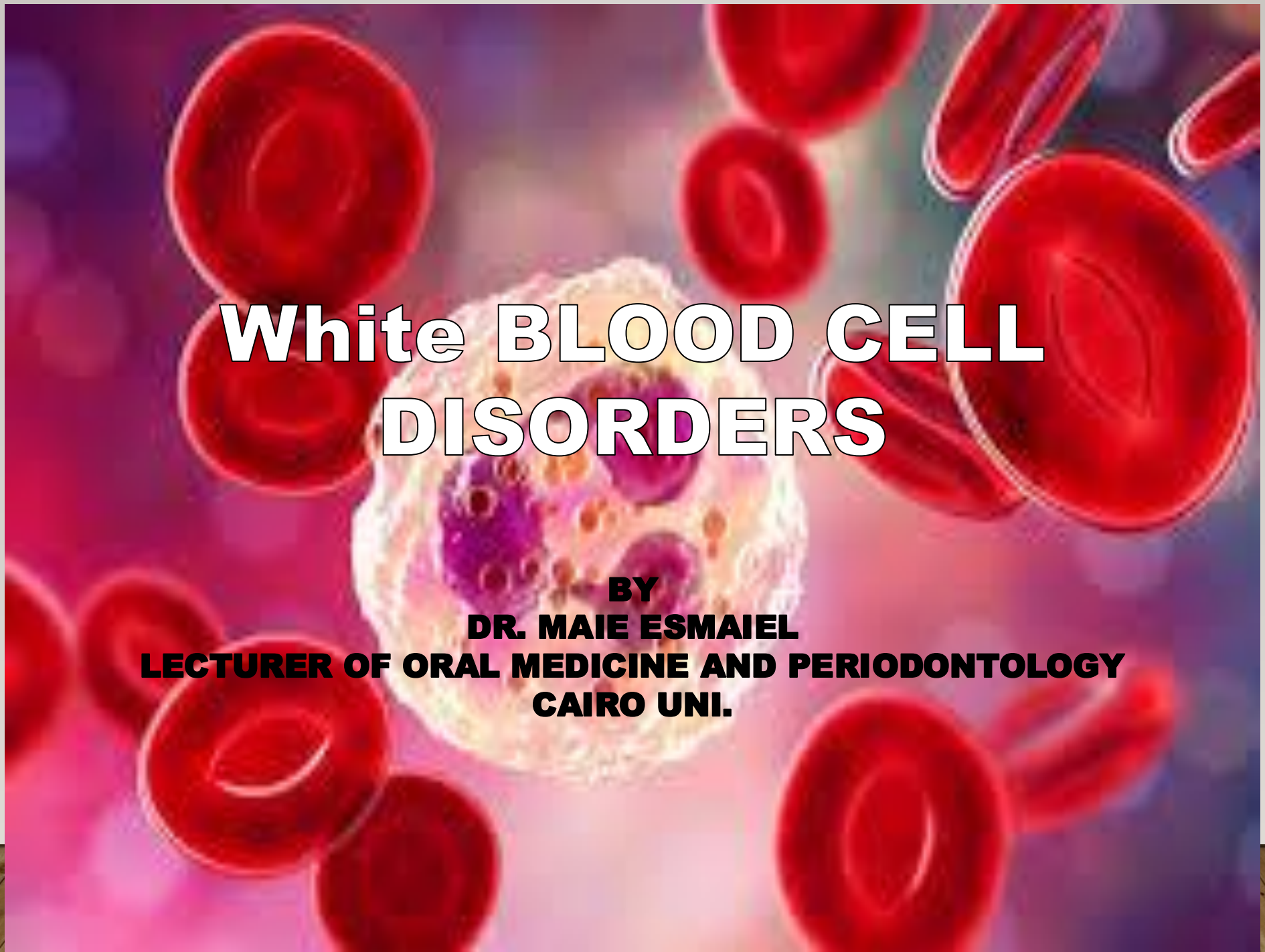

White BLOOD CELL DISORDERS

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WHITE BLOOD CELL DISORDERS

WBCs count:

Total leukocytic count

- 4000-11000 white cell / mm^3

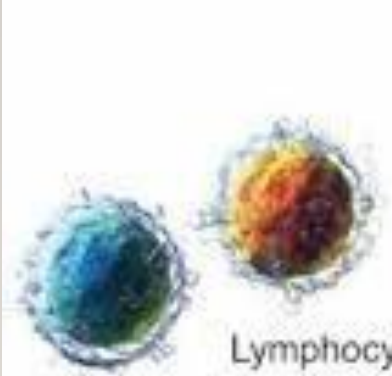
Differential leukocytic count

- **Segmented neutrophils :** 3000 - 6000/mm^3
- **Lymphocytes :** 1500 - 4000/mm^3
- **Monocytes:** 200 - 900/mm^3
- **Eosinophils :** 100 - 700/mm^3
- **Basophils :** 20 - 150/mm^3

Leukocytes
(white blood cells)

agranular

granular



Lymphocytes
20-25%

Monocyte
3-8%

Basophil
0.5-1%

Neutrophil
60-70%

Eosinophil
2-4%

Classification:

(1) Quantitative defects:

- Agranulocytosis
- Cyclic neutropenia

(2) Qualitative defects:

- Infectious mononucleosis
- Multiple myeloma
- Leukemia
- Lymphoma

Neutrophils

- Neutrophils are the first line of defense against bacterial invasion of the mucous and bactericidal action.

- This function is aided by immunoglobulin and complement.

Monocytes

- Monocytes are immature cells when, in the blood stream but once they reach the tissues they become mature phagocytes (marophages).

Eosinophils

- Eosinophils may phagocytes foreign substance but **cannot kill bacteria.**

Basophils

- Basophils migrate to tissues and act as mast cells in allergic reactions.

Lymphocytes T & B

- Lymphocytes T & B are involved in cellular and humoral immunity.

Definition of terms:

Leukocytosis:

- Increase in number of leukocytes more than 11.000/mm^3

Leukopenia:

- Decrease in number of leucocytes less than 4000/ mm^3

Agranulocytosis:

- Absence of neutrophils in peripheral blood

Granulocytopenia (neutropenia):

- Decrease in number of granulocytes mainly neutrophils.

Leukemoid reaction:

- Persistent elevation of white blood cell count with absolute neutrophil count remaining above 30,000/mm^3, (e.g. viral infection).
- The cells are mature.
- Bone marrow biopsy is required to differentiate leukemoid reaction from leukemia.

Agranulocytosis vs Cyclic neutropenia

Agranulocytosis	Cyclic neutropenia
No neutrophils are found in peripheral circulation.	• Periodic or cyclic decrease of circulating neutrophils secondary to bone marrow maturation arrest.
Etiology	
1- Idiopathic.	
2- Secondary to: drugs, irradiation, severe infection.	• Neutropenic episodes: occur every 3-4 weeks and last for a few days (3-5)

Clinical Features.

- **Age: adult**
- **Sudden onset of fever, chills, sore throat and lymphadenopathy.**
- **Infection: Common sites include gastrointestinal tract (GIT), urinary tract and lung.**

Clinical Features.

- Age: infant and childhood.
- The patient is healthy between the attacks (neutropenic episodes). Neutrophil count falls below $500/mm^3$ or even to zero during the attack. The neutropenic episode stays for 4 days and occurs every 21 day.

- Fever, sore throat and lymphadenopathy but milder than agranulocytosis.
- Infection is less frequent because:

ii- There is compensatory ↑ in monocytes.

iii- The neutropenia is periodic.

Oral features:

•Oral ulcers which are:

*** Large** *** Necrotic**

*** Deep** *** Foul odour (due to fusospirochetal infection)**

*** Irregular** *** Painful**

*** Lack inflammatory halo.**

- **Regional lymphadenopathy (common)**

Oral features

1- ***Oral manifestations:***

1-During neutropenic episode:

a. Severe gingivitis.

b. Stomatitis with oral ulceration both are due to bacterial invasion. These return to normal when neutrophilic count returns to normal.

2- Repeated gingivitis may progress to periodontitis or rapidly progressive periodontitis.

3- There may be isolated major aphthous-like ulcers (patient with such ulcers, cyclic neutropenia should be ruled out).

Lab. Finding

- **Peripheral blood smear:**

1- Absence of granulocytes

2- Total W.B.Cs ⩽ 2000/cu mm.

- **Bone marrow: normal but granulocytes are absent.**

Treatment

- **Eliminate cause.**

Management

- **Parenteral antibiotics**
- **Keep mouth and skin as clean as possible by:**

1- Chlorhexidine mouwash.

2- Topical antibiotic.

*** No dental surgery should be performed**

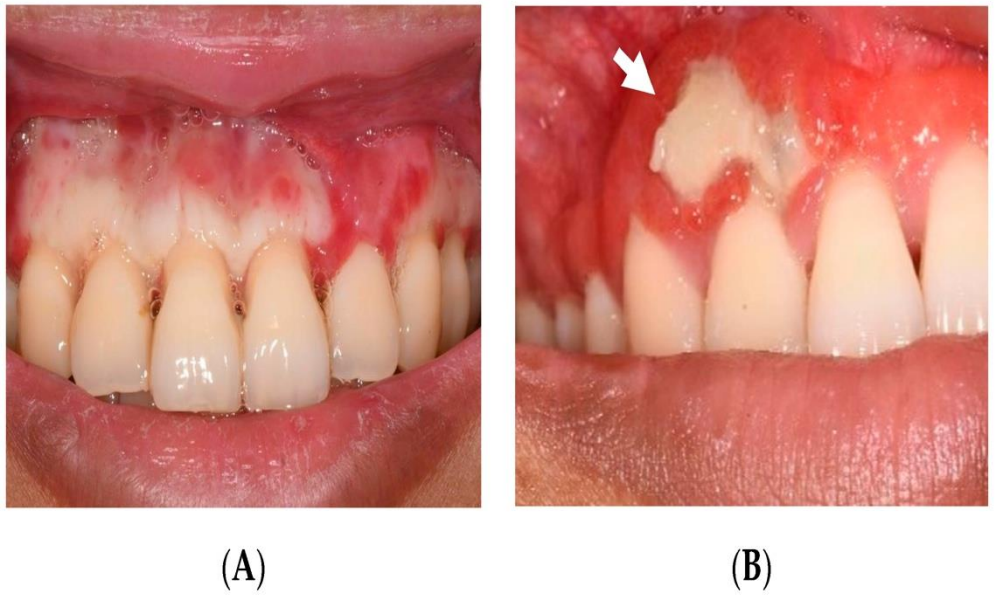
Lab. Finding

- Periodic decrease in circulating neutrophils.

Management

- Maintain good oral hygein.
- Periodic recall for periodontal treatment.

AGRANULOCYTOSIS



CYCLIC NEUTROPENIA

Infectious Mononucleosis

Infectious Mononucleosis (Kissing disease-Glandular Fever)

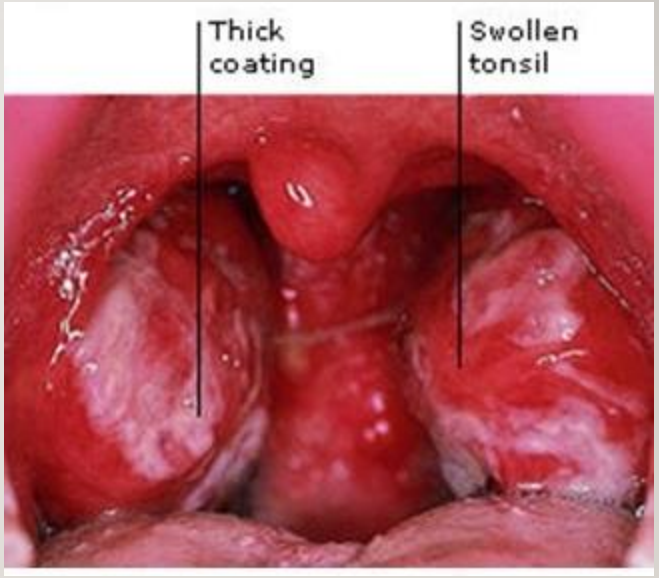
Definition:

- It is self limiting disease occurs predominantly in children and adults and is caused by Epstein-Barr virus (EBV). The saliva is loaded with the virus so the disease spreads by oral contact.
- It is also called kissing disease because of occurrence in younger age group

Clinical features:

1. Fever, headache and malaise.
2. Generalized lymphadenopathy particularly the posterior deep cervical.
3. Spleenomegaly.
4. **Oro-pharyngeal features:**

    A. Acute onset of sore throat with exudates on the tonsils.
    B. Petechiae at the junction of hard and soft palate.
    C. Pharyngeal edema which may threaten the airway

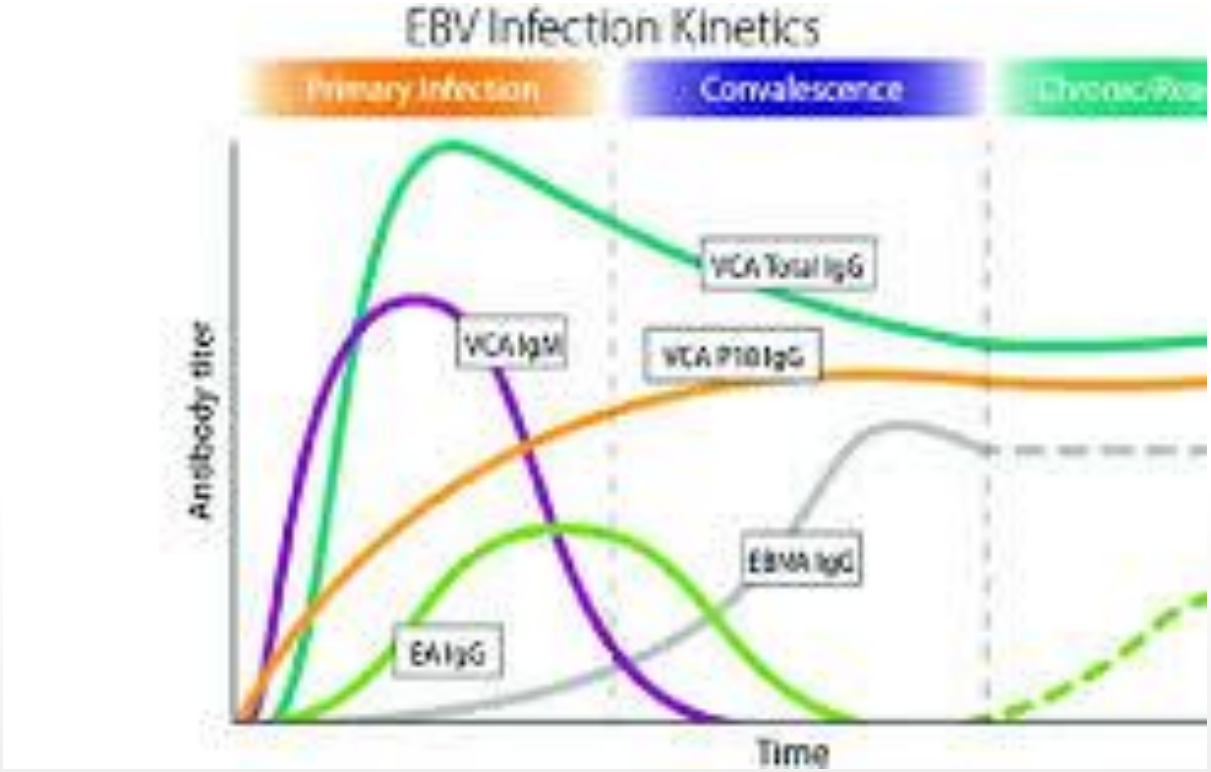

Thick coating
Swollen tonsil

Laboratory investigation:

1. ***Lymphocytosis:*** increased number of lymphocytes may represent up to 80% of the leukocytic count.

2. ***Atypical lymphocytes:*** They have pseudopodia that project from the cell.

3. ***EBV antibodies*** are detected against viral capsid antigen. EBV antibodies are produced in the disease and persist for many years..


EBV Infection Kinetics
Primary Infection
Convalescence
VCA Total IgG
VCA IgM
VCA P18 IgG
EBNA IgG
EA IgG
Antibody titer
Time

4. Heterophil antibodies(IgM); detected by:

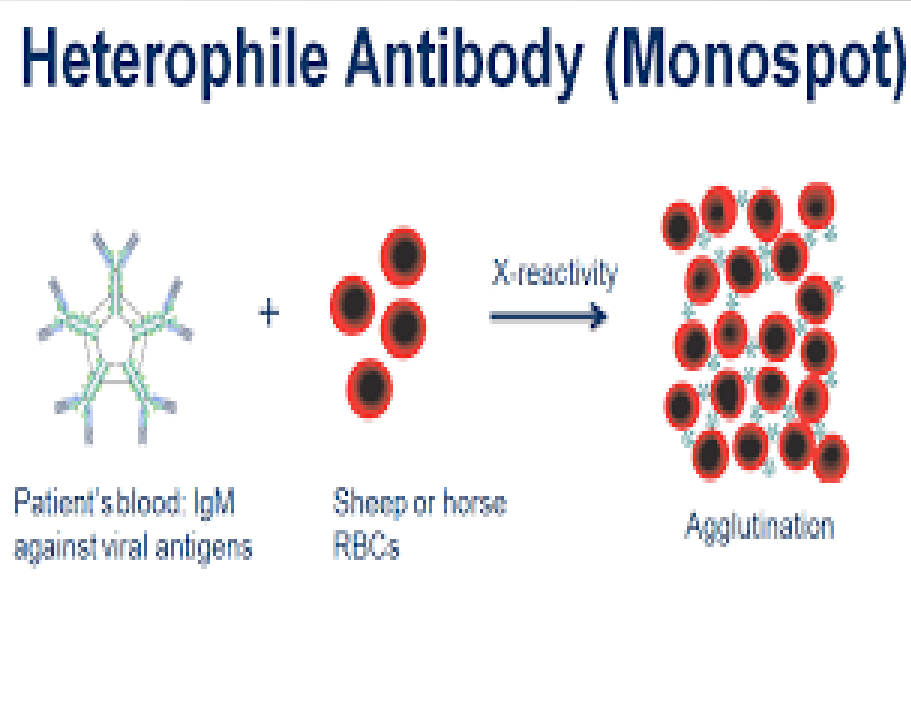
- ***Paul bunnel test:*** Antibodies agglutinate sheep RBCs.
- ***Monospot test:*** Antibodies agglutinate hoarse RBCs.
  - The titre of heterophil antibodies develop by 1-2 weeks of the illness and disappear over 3-6 months

Treatment:

- **Mainly Symptomatic**
- **Systemic steroid for severe laryngeal edema**
- **Flagyl for sore throat**
- **Antiviral drugs in severe cases.**

HETEROPHIL ANTIBODIES

- Heterophile antibodies are IgM antibodies produced against poorly defined antigens.
- These are generally weak antibodies with multispecific activities, with affinity for sheep and horse red blood cells.
- They appear during the first week of infectious mononucleosis ...
-



Multiple Myeloma

Multiple Myeloma

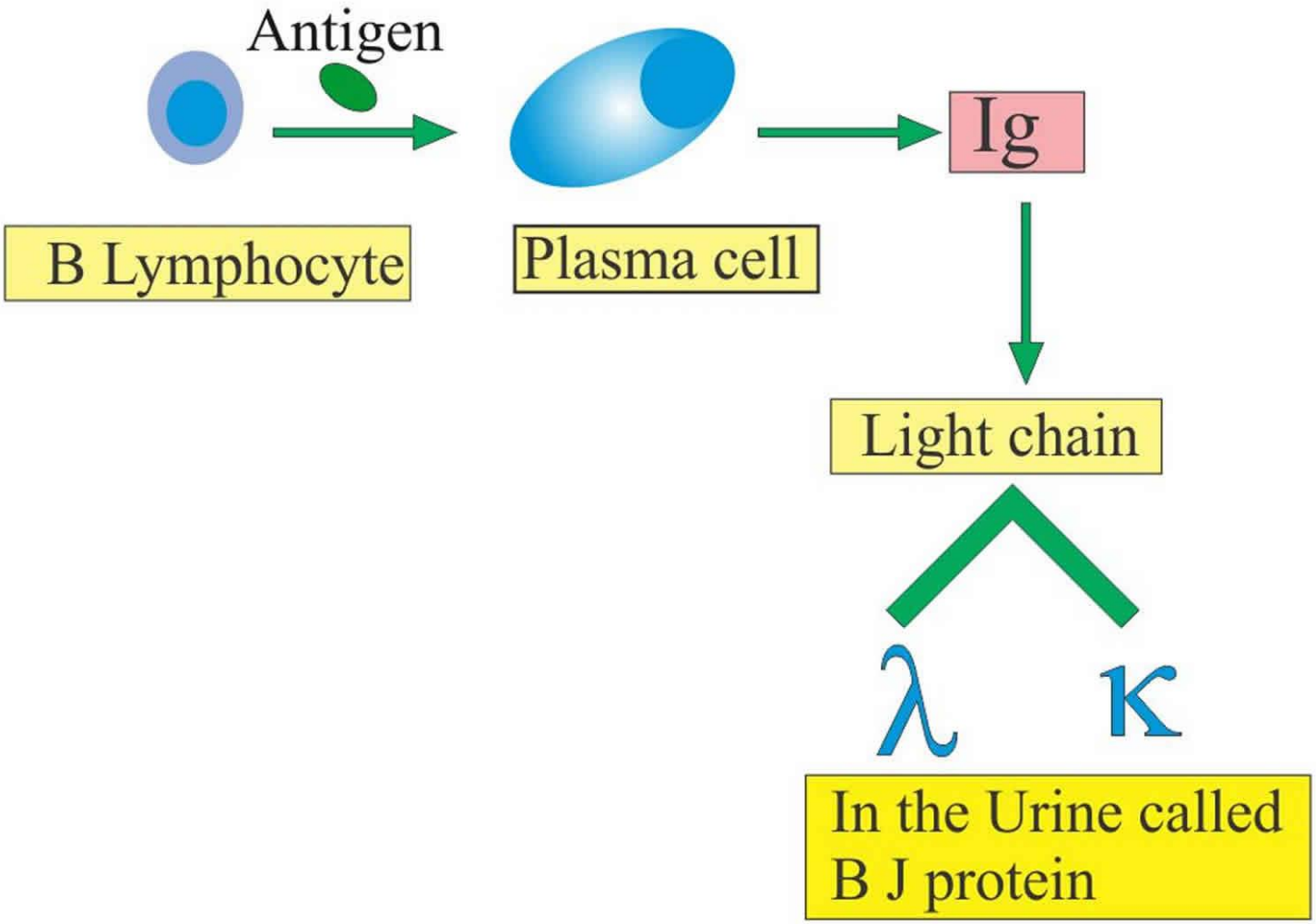
Definition

- It is disseminated **plasma cell neoplasm in the bone marrow** producing abnormal monoclonal immunoglobulin (IgG less commonly IgA).
- This paraprotein can be detected in the blood and urine (by their electophoretic pattern) and in urine **(Bence Johns Protein).**

Bence-Jones proteins are a part of regular antibodies called light chains. These proteins are not normally in urine.

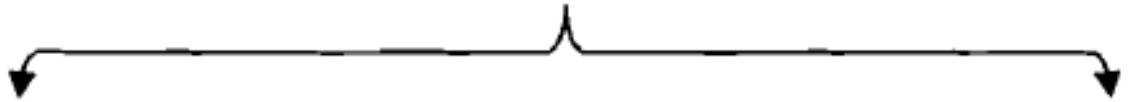
Sometimes, when your body makes too many antibodies, the level of light chains also rises. Bence-Jones proteins are small enough to be filtered out by the kidneys.

Bence Jones protein



Pathogenesis:

The malignant plasma cells:



Produce abnormal antibodies

(M protein)

infiltrate body tissues

Defective	Bind	Coat	High
defensive	clotting	platelets	viscosity
mechanism	factor		

The neoplastic plasma cells will lead to:

1-Bone marrow infiltration resulting in:

- Anemia
- Thrombocytopenia
- Neutropenia

(Pancytopenia)

2-Bone destruction causing fractures, vertebral collapse and hypercalcemia

3-Renal impairment secondary to:

- **Deposition of light chains** of the paraprotein in renal tubules
- Invasion of the kidney by neoplastic cells.

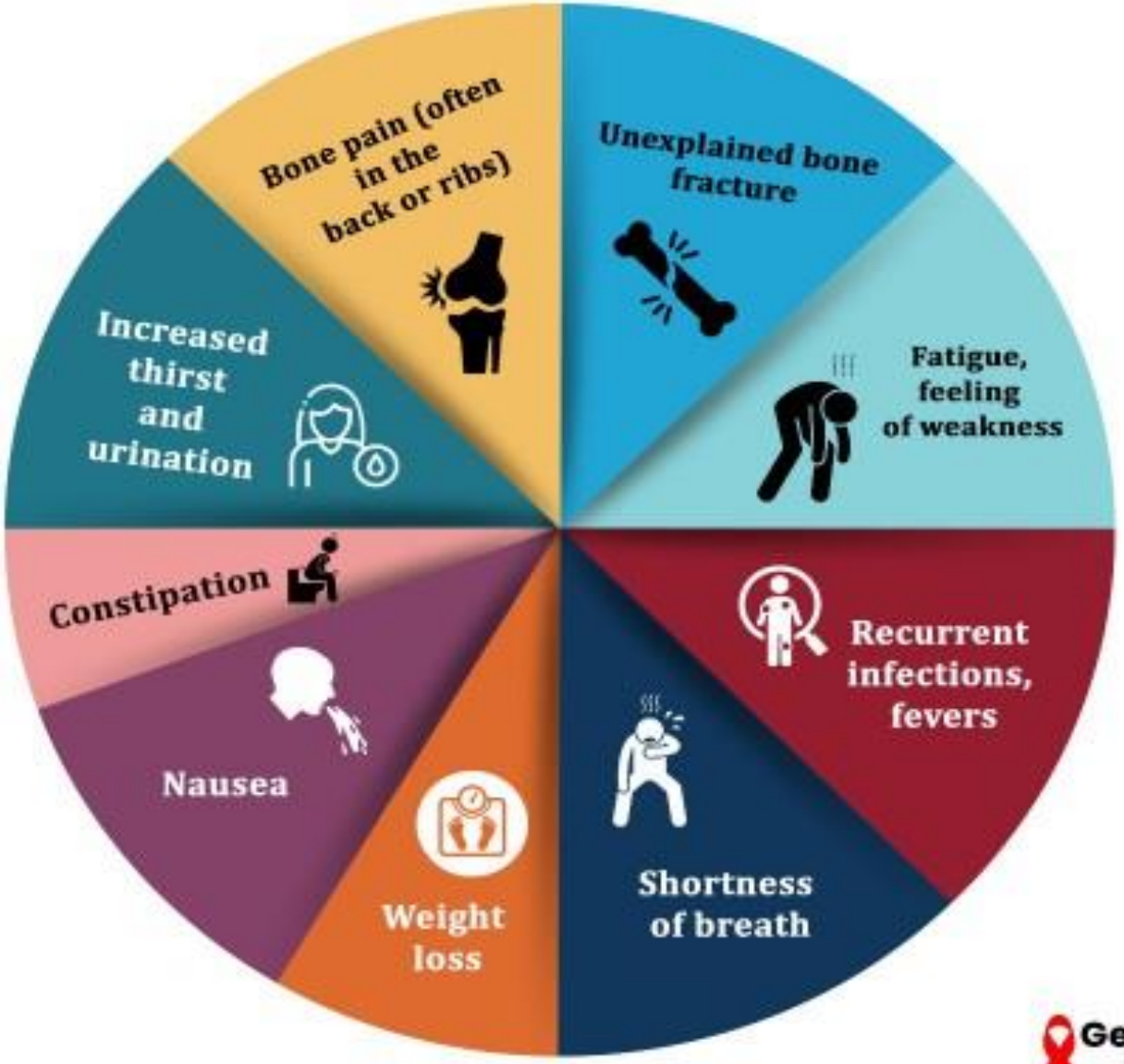
4. The paraprotein can:

- Bind with the **clotting factors**, render them inactive and may lead to increased liability to bleeding.
- Increase the **blood viscosity**.
- Coat the platelets resulting in **defective platelets function..**

Clinical features

- Bone pain
- Spontaneous pathological fracture,
- Anemia,
- Excessive bleeding tendency
- Neurological lesions as paraesthesia
- Weakness and visual disturbance.

Multiple myeloma symptoms



GenericForce
A Lifesaving Force

C	R	A	B
High levels of calcium in the blood	Decreased kidney (renal) function	Low amount of red blood cells (anemia)	Presence of bone damage

Oral manifestations may be the first sign of the disease and characterized by:

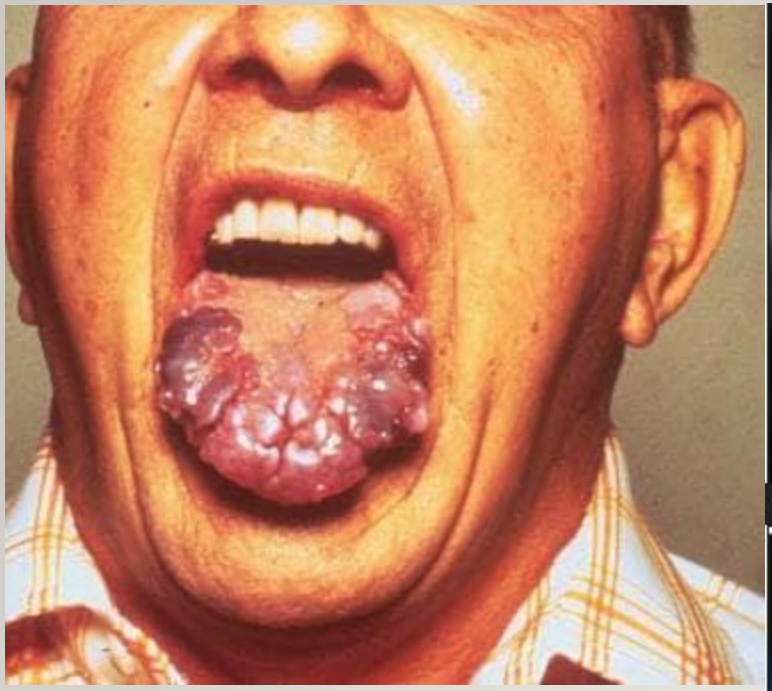
1.Infiltration of jaws by malignant plasma cells which results in:

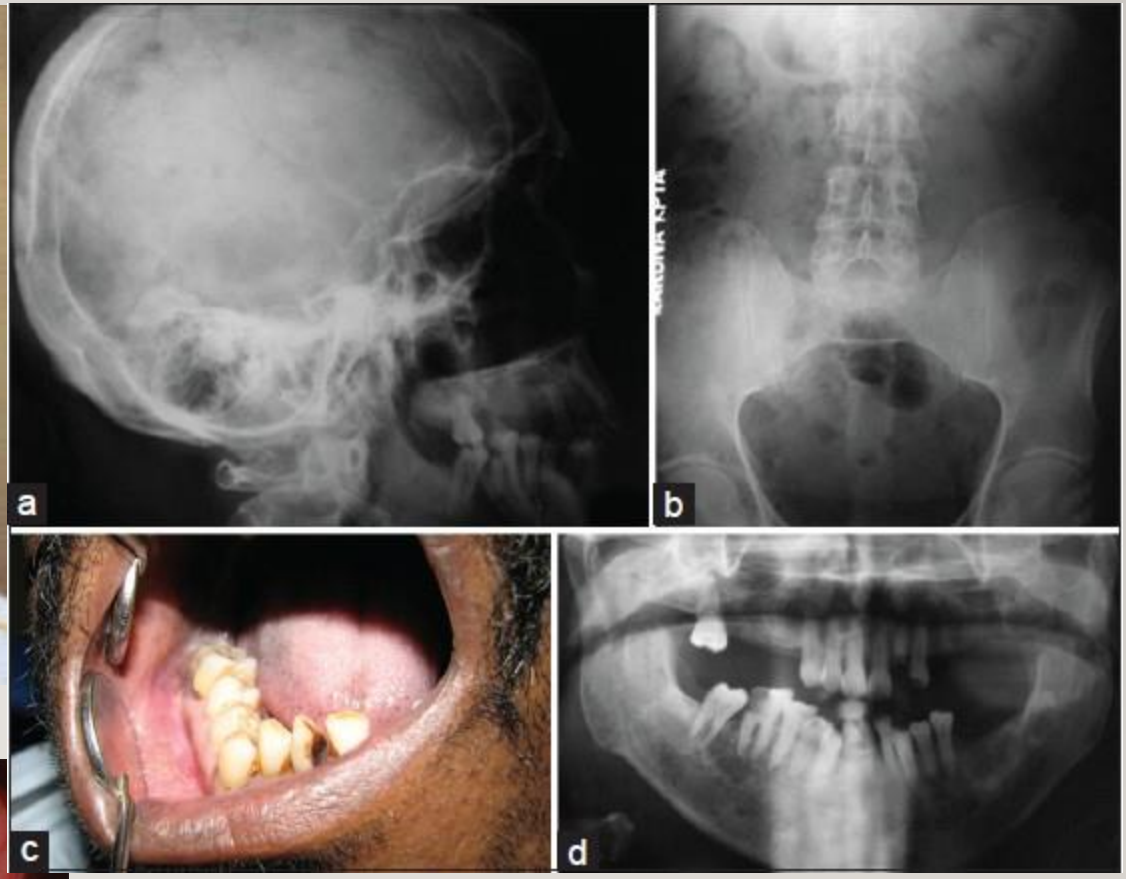
- Numbness.
- Pathologic fracture.
- Mobility or migration of the teeth.
- III-defined multiple radiolucent lesions.
- Pain in the jaw or teeth
- Amyloid deposition of the tongue (macroglossia).

2. Infiltration of oral soft tissue.

3. Infiltration of bone marrow by malignant plasma cells which results in:

- Pallor of oral mucosa
- Bleeding tendency
- Increased susceptibility to infection




a
b

c

d

L
AC

Radiological findings

- Generalized osteoporosis
- Punched out radiolucency

Laboratory features

Hematological

- Normochromic anemia
- Neutropenia
- Thrombocytopenia

Diagnosis

1. Protein electrophoresis: characteristically show monoclonal band (serum and urine).

2. Urine: for assessment of light chain excertion.

3. Detection of plasma cell neoplasia bone marrow biopsy.

4. X-ray: Generalized osteoporosis or punched out osteolytic lesion (skull).

Dental management complicated by:

1-Hemorrhage resulting from

- Thrombcytopenia
- Abnormal platelets function
- Abnormal coagulation
- Hyperviscosity

2-If surgery is necessary blood investigation should be performed:

- Platelets count
- Bleeding time
- PTT
- PT

3-Increased susceptibility for infection due to:

- Neutropenia
- Abnormal immunoglobulin
- Bone marrow failure
- Cancer chemotherapy

4-Renal Failure, anemia & chemotherapy may complicate dental management.

Leukemias

Leukemias

Definition

- Leukemias are malignant neoplastic proliferation of white blood cells…..(lymphoid, monocytic or myeloid stem cells) and characterized by the presence of immature cells in the peripheral circulation and bone marrow (in high percentage).

Classification

Leukemia is classified according to:

1-Speed of evolution and clinical course

	Acute leukemia	Chronic leukemia
Onset	Rapid	Gradual
Survival time	<6 m.	Many years
Cells	Immature (…blast)	Well differentiated (… cyte)
Clinically	Very severe	Less severe
Age	Young	Old

2-According to the individual cell:

- Acute myelogenous leukemia most common in adult	-Acute lymphoblastic leukemiamost common in childhood (3-5)years
-Chronic granulocytic(myeloid) leukemia.	-Chronic lymphocytic leukemia

3-According to the number of circulating leukemic cells:

a-Aleukemic leukemia:

- Normal number of WBCs in peripheral circulation.
- **No immature cells in peripheral circulation.**
- Bone marrow crowded with immature WBCs.

b-Subleukemic leukemia:

- Normal number of WBCs.
- Immature cells are present in peripheral circulation.

c-Leukemic leukemia:

- Increased number of WBCs in peripheral circulation.
- Immature cells are present in peripheral circulation.

Etiology

1. ***Genetic factor:*** Chromosomal abnormalities e.g Philadelphia chromosome have been associated in 95% of cases of chronic myeloid leukemia. It results from translocation of genetic material from chromosome 22 to chromosome 9.

2. ***Environmental factors:***
   - Radiation (radiotherapy, radiation of atomic bombs).
   - Drugs: cytotoxic drugs.
   - Chemicals: benzene compound used in industry.
3. ***Viral factors:*** Human T leukemia virus (HTLV).

Clinical features.

Generally the signs and symptoms ofleukemia are due to:

1-Suppression of the bone marrow by leukemic cellswhich may result in:

- Anemia.
- Thrombocytopenia.
- Impaired normal function of neutrophils: impaired function of immune system (B or T lymphocytes).

2-Infiltration of leukemic cells in various tissues:

- Liver
- Spleen
- Lymph nodes
- Gingiva.

3-Chemotherapy used for treatment of leukemia.

General features:

1. Anemia

- Pallor
- Headache
- Dyspnea on exertion fatigue
- Palpitation and tachycardia

2. Features of thrombocytopenia:

- **Petechia:** small purpura (purplish macule due to extravasation of blood)
- **Ecchymosis:** large purpura.
- **Epistaxis:** bleeding from the nose.

3. Features related to normally function leukocytes:

- Fever
- Infection urinary tract, GIT and lung.

4. Features related to infiltration of leukemic cells in various tissue:

- Hepatospleenomegaly.
- Lymph node enlargement.
- Infiltration of nerve tissue numbness & paralysis

Oral manifestation

- Oral manifestations of acute and chronic leukiemias are the same, generally chronic leukemias are less severe. ***Oral manifestations are due to:***

1. **Bone marrow suppression** (anemia and thrombocytopenia).
2. **Leukemic cellular infiltration** in various tissues and organs which impairs their function.
3. **Impaired function** of immature granulocytes, B-T lymphocytes and neutrophils.
4. **The use of anticancer drugs**

Oral features include:

1. Features of anemia:

- Pallor
- Atrophy of tongue coating.

2. Features of thrombocytopenia:

- Petechia.
- Ecchymosis.
- Bleeding from the gingiva.

3. Features related to normally function leukocytes:

- Candidal
- Bacterial Mainly due to impaired T and B cell function and neutropenia

4. Features related to infiltration of leukemic cells in various oral tissues:

- Gingiva gingival enlargement.
- Pulp odontalgia (pain in the teeth without observable cause).
- Alveolar bone osteomyelitis.
- Cervical lymph node lymphadenopathy.
- Periodontal ligament Teeth extrusion, loosness and rapid loss of teeth

- **Cranial nerves:**
  - Facial nerve involvement Bells palsy
  - Trigeminal nerve involvement trigeminal neuralgia.
- **Xerostomia and enlargement of parotid gland**

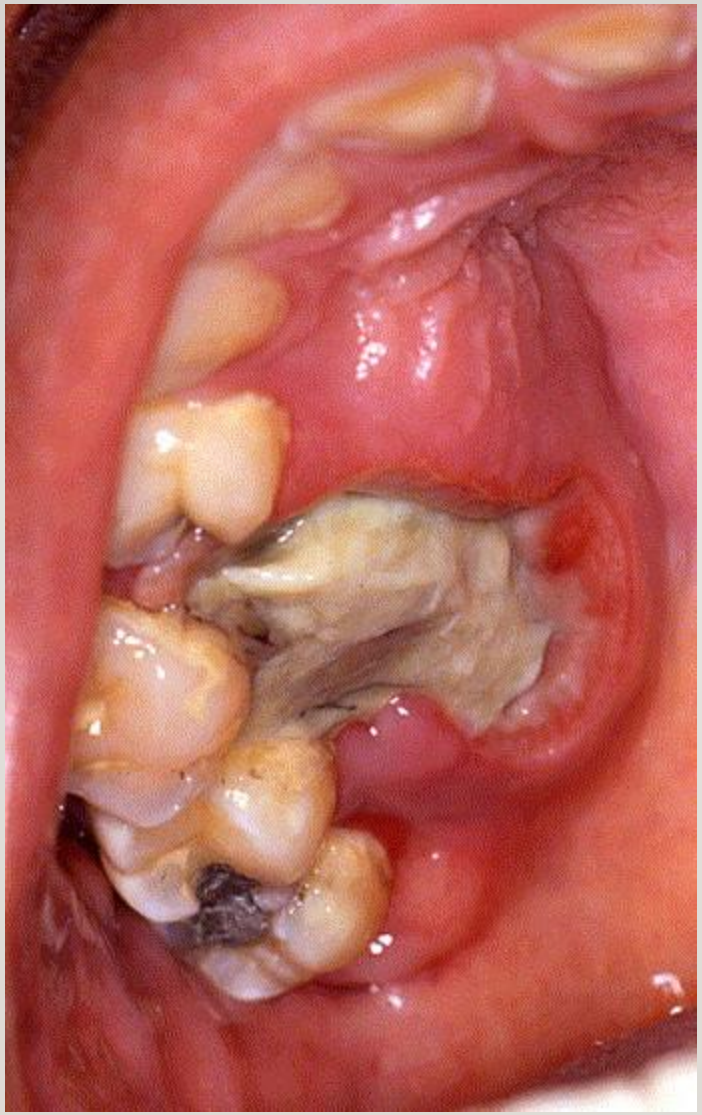
A

B

5. Features related to chemotherapy:

Oral ulcers:

- Large Deep.
- Necrotic Foul odour (due to fusospirochetal infection).
- Painful Irregular.
- No inflammatory halo.



N.B.: Bleeding tendency in patient with leukemia is due to:

- Thrombocytopenia.
- Defect in synthesis of clotting factors due to liver infiltration.
- If there is synthesis of clotting factors, they are consumed due to formation of disseminated intravascular coagulation (DIC).

Dental implications:

1. Conservative dental therapy, while avoiding oral surgical procedures. If the latter is inevitable, the patient should be hospitalized

2. Oral hygiene should be encouraged with regular 0.2% chlorhexidine mouth rinse. Antifungal and antiviral drugs can be prescribed as prophylactic

3. Every effort should be done to avoid extraction, ***so:***

   - Maintain good oral hygiene.
   - Regular check up

4. Prophylactic antifungal drugs or antiviral drugs

5. Root canal treatment for management of odontalgia.

6. Any infection has to be treated immediately as may be fatal.

7. Topical anaesthesia for oral ulceration.

8. Stop gingival bleeding by:

   - Pressure pack.
   - Topical application of thrombin

- If the local measures fail, refer the patient to the hospital for blood transfusion or platelets transfusion

9. The infection is less problematic in patients with chronic leukemia, than those with acute leukemia.

- This is because the cells are more mature and functional in chronic leukemia.
- However, in later stages, infection becomes a serious complication.

10. With special consideration, patients who are in a state of remission can receive most of the indicated dental treatment.

    - For periodontal and surgical procedures, bleeding should be undertaken beforehand, if bleeding time is prolonged, delay dental treatment or obtain platelet replacement through consultation with the patient's physician.

11. Operative procedures should be performed with strict asepsis and as atraumatically as possible with the use of synthetic absorbable suture materials.

12. Aspirin should be avoided since it may interfere with hemostasis.

Lymphomas
WallpapersMania

Lymphomas

- Lymphomas are group of malignant tumors of lymph nodes and lymphoid tissues

Classification of lymphoma

- Lymphomas are classified according to histopathological features into:

1-Hodgkin's disease

A. Lymphocyte predominant (best prognosis)
B. Nodular sclerosis

Younger patient

A. Mixed cellular }
B. Lymphocyte depleted (worst prognosis)

Older patients

2- Non Hodgkin's lymphoma

- Nodular
- Diffuse (including Burkett's lymphoma)

1-Hodgkin's disease

A. It begins in younger patients, 20-30 years of age as asymptomatic enlargement of peripheral lymph nodes, most commonly the cervical (60-70%).

B. The lymph nodes are enlarged, discrete, rubbery and not tender to palpation.

C. In older patients, systemic symptoms may precede lymphadenopathy.

D. Systemic symptoms include pain, fever, night sweats, weight loss, malaise, bone pain and pruritis.

- The enlarged lymph nodes can cause symptoms by pressure on other organs or ducts.
- Enlargement of mediastinal nodes causes dysphagia and retroperitoneal nodes cause urinary obstruction.

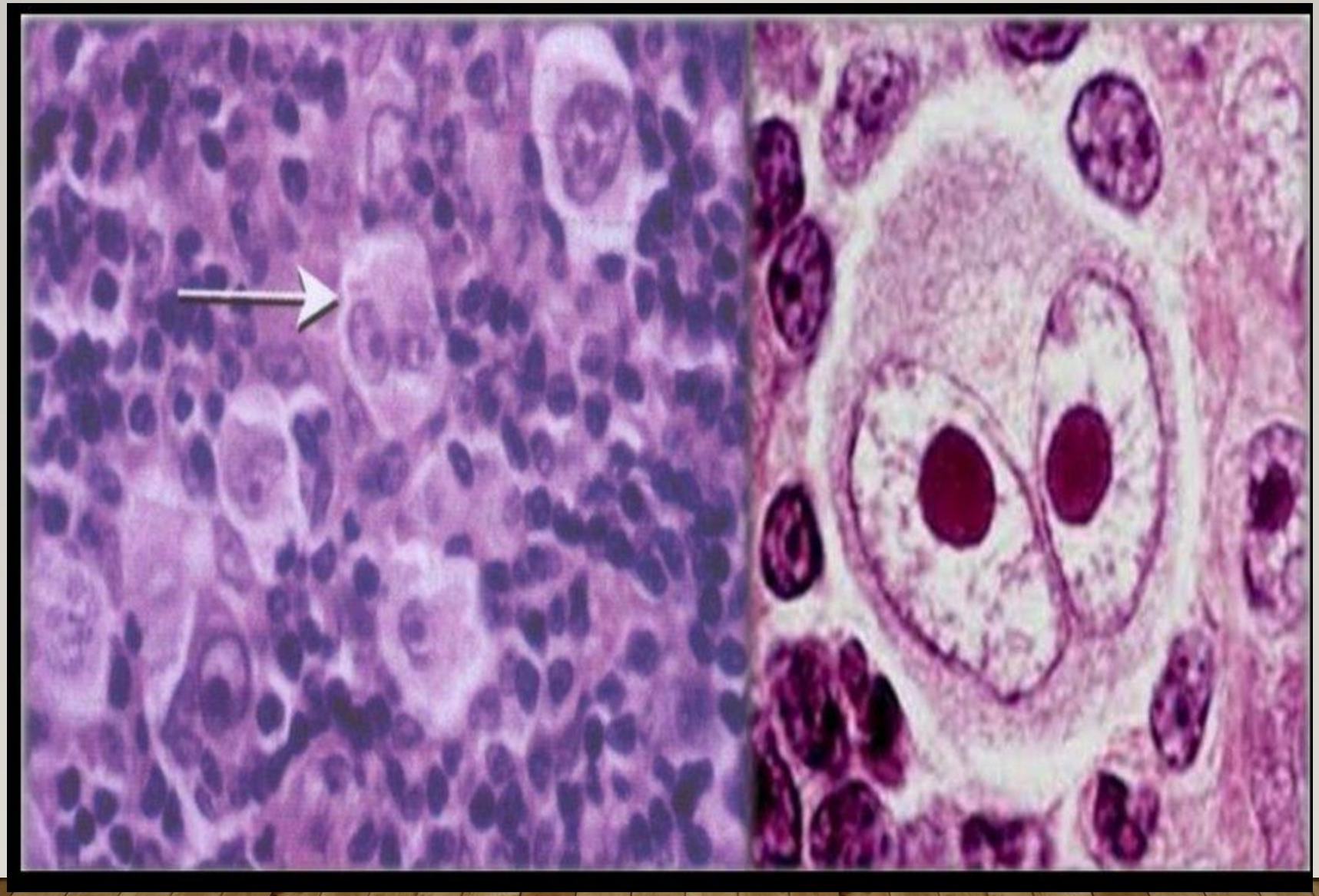
- Further progression of the disease leads to invasion of bone marrow, spleen, skin, liver, lung and spinal cord.
- Anemia is common, late in the disease.
- Cellular immunity is impaired with loss of T-cell function that worsens as the disease progresses, so fungal and viral infections are common and maydisseminate.

Treatment

- Chemotherapy and radiotherapy or combination used for treatment may suppress neutrophils and antibody function for years, increasing the patient's susceptibility to bacterial infection.

Diagnosis

- Definite diagnosis is mainly reached by biopsy. They presence of characteristic Reed Sternberg cells is diagnostic which is described as having mirror image nuclei with owl eye nucleoli.



2-Non Hodgkin's lymphomas

- NHL seen in patients over 40 years and generally have poor prognosis.. The most common presentation is painless enlargement of lymph nodes, the cervical being common and is the first sign and Waldeyer's ring, gastrointestinal tract and CNS lymph nodes

Treatment

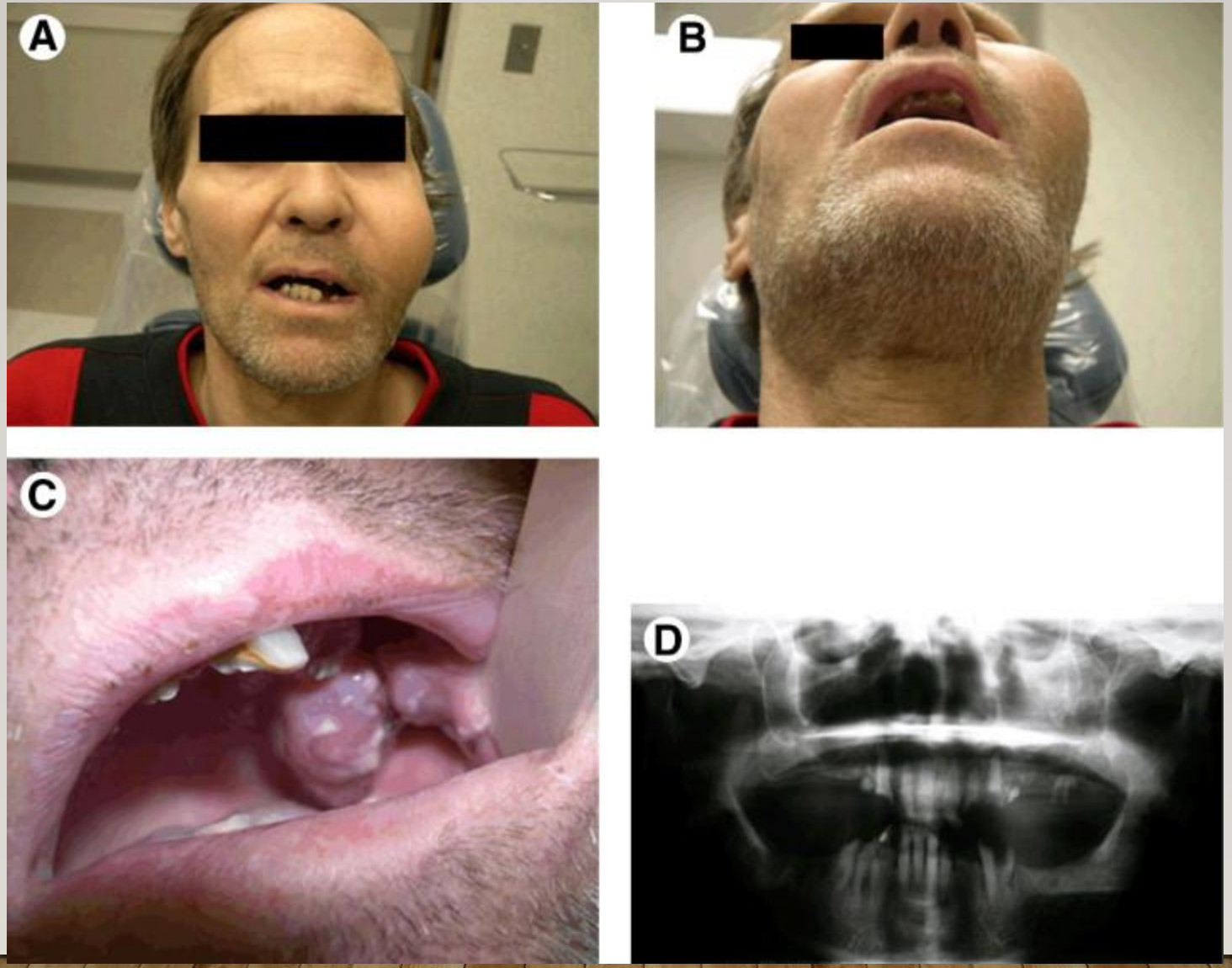
- Since early dissemination of NHL is common, NHL is treated with multiple chemotherapy. Radiotherapy may be useful in the intial stage.

Dental aspects and management problems of lymphomas

- Painless enlargement of cervical lymph nodes may be the initial manifestation ofthe disease.

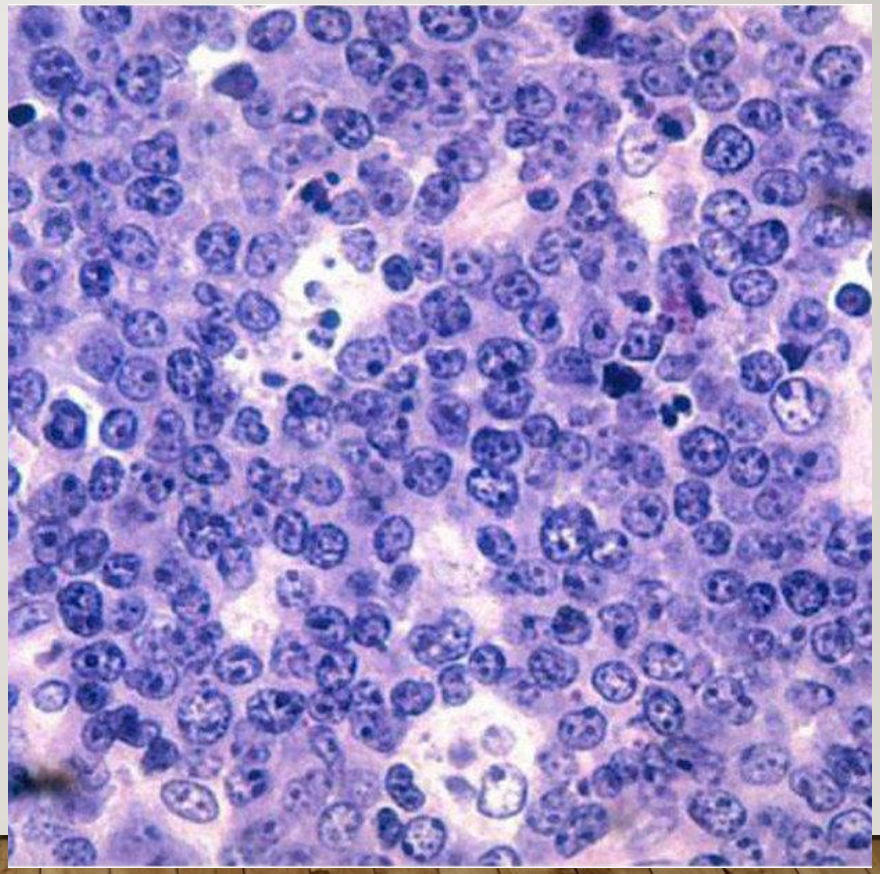
- Extranodal involvement of Waldeyers ring (palatine, pharyngeal and lingual tonsils) is more common in NHL than Hodgkin's disease. Non tender enlargement of the tonsillar tissue in adult should be referred to otolaryngologist for evaluation.

- Hodgkin's disease rarely affects the mouth.
- NHL may reveal soft tissue swelling in pharynx, palate, tongue, gingival or lips.
- The jaw bones may be involved (Burkitt's lymphoma) and the teeth may become losse.


A
B
C
D

The Starry-sky pattern of Burkitt's lymphoma.

The tumor cells of B lymphoblasts which are large rounded or indented nucleus and 3 or 4 nucleoli with thin layer of basophilic cytoplasm are closely apposed to each other forming a dark blue background (the 'sky'). The surrounding macrophages with abundant pale foamy cytoplasm scattered among the tumor cells (the stars).



- Oral infection with viruses, fungi or bacteria may occur as a result of depressed T or B cell function.
- Oral ulceration may be induced secondary to cytotoxic drugs.
- Anemia and bleeding tendencies are due to malignant cell infiltration of bone marrow and or the effect of cytotoxic drugs.

THANK YOU..